REMARKS

Upon entry of the present amendment, claims 44-50, 56 and 59 - 62 are pending, with claims 51 – 55, 57 and 58 withdrawn. Claims 1 – 43 have been cancelled. Claim 44 has been amended to more clearly define the present invention. Basis for the amendment can be found in the Specification as originally filed, and in particular in Example 2. New claims 60 – 62 have been added to cover subject matter deleted from claim 47. No new matter has been added by the present amendment.

THE 35 U.S.C. §112, SECOND PARAGRAPH REJECTIONS

The Examiner has rejected claims 44 – 50, 56 and 59 under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants have amended claims 44 and 47 cancelled claims 19 – 21, 23, 24, 27, 42 and 43 and added new claims 44 – 59. Accordingly, Applicants believe that the present rejection is now moot.

THE 35 U.S.C. §112, FIRST PARAGRAPH REJECTIONS

The Examiner has rejected claims 44 – 59 under 35 U.S.C. §112, second paragraph as failing to comply with the written description requirement.

Applicants have amended claim 44 to more clearly define the present invention as suggested by the Examiner. Basis for the amendment can be found in the Specification as originally filed, and in particular in Example 2. Accordingly, Applicants believe that the present rejection is now moot.

THE 35 U.S.C. §102(B) REJECTIONS

The Examiner has rejected claim 44 – 47, 50 and 56 under 35 U.S.C. §102(b) as being clearly anticipated by Park *et al.*, alleging that it discloses *in vitro* methods of culturing and maturing oocytes in a culture medium containing EGF and sperm and allowing zygotes to develop.

Applicants traverse. Applicants note that the results described in Park *et al.* do not teach or disclose data supporting the effect of EGF on oocyte maturation. In contrast, the reference actually emphasizes that the effects from the basal medium used serve to mature the oocytes. This is clearly

illustrated by comparing the results of Table 3 with that of Table 4. Specifically, Table 3 is directed to the frequency of oocyte maturation in which oocytes has been matured with EGF (35.8% cleavage rate), while Table 4 is directed to the frequency of oocyte maturation in which the oocytes were not treated with EGF (50% cleavage rate). The disclosed differences in cleavage rate are merely insignificant changes, suggesting that the differences observed rely on other factors such as the medium composition. In addition, Applicants note that the results in Table 2, in which EGF was added to the medium, is similar to the results given in Table 3, in which EGF was not added, again suggesting that it is factors other than EGF that caused the observed differences in oocyte maturation. Thus, Applicants assert that Park *et al.* does not anticipate the claimed invention. Accordingly, Applicants request reconsideration and withdrawal of the present rejection.

The Examiner has rejected claim 44 –50 under 35 U.S.C. §102(b) as being clearly anticipated by Illera et al., alleging that it discloses the maturation and culturing of oocytes ina medium which contains EGF, FSH and sperm, and allowing zygotes to develop.

Applicants traverse. Applicants note that Illera *et al.* discloses the use of fetal calf serum (FCS), which is commonly known by those skilled in the art to contain many different substances that can interfere with results. Moreover, the results described in Illera *et al.* clearly demonstrate that when exogenous hormones, such as FSH and LH, are added to the culture medium, the fertilization rate actually decreases upon the addition of both EGF and IGF-1. In fact, only when FSH and LH, plus porcine follicular fluid are left out of the medium, do EGF in combination with IGF1 augment the fertilization rate. This is in direct contradiction to the present invention and thus, teaches away from the addition of both EGF and FSH. Applicants also note that the present invention does not comprise the use of IGF1. Most importantly, Applicants note that it is not possible to use FCS in a clinical setting for the purpose of oocyte maturation in an in vitro method of fertilization. Thus, Applicants assert that Illera *et al.* does not anticipate the claimed invention. Accordingly, Applicants request reconsideration and withdrawal of the present rejection.

THE 35 U.S.C. §103(A) REJECTIONS

The Examiner has rejected claims 44 – 47, 50, 56 and 59 under 35 U.S.C. §103(a) as being unpatentable over Ben-Yosef *et al.*, alleging that it discloses a method of *in vitro* fertilization

comprising induction of ovulation (maturation) *in vivo* by injection of that intact animal with PMSG and hCG, harvesting the oocytes, incubating them with EGF and then transferring them to a sperm suspension.

Applicants traverse. Applicants note that the present reference actually employs intact follicles from rats. In contrast, the present invention uses isolated oocyte-cumulus complexes. This is two completely different entities, composed of completely different cells in a different environment, that may behave totally different when exposed to different hormonal signals because they may express hormone receptors. It is therefore not obvious to the skilled person that results obtained in one system would apply to the other system. In addition, it is important to note that in a clinical setting, it is impossible to obtain intact follicles comparable to those used in the study of Ben-Yosef *et al.* from human ovaries. In order to obtain such follicles it would most likely be needed to remove the ovary from the woman and therefore not an option. Thus, Applicants assert that Ben Yosef *et al.* does not render the present invention unpatentable. Accordingly, Applicants request reconsideration and withdrawal of the present rejection.

The Examiner has also rejected claims 44 – 50, 56 and 59 under 35 U.S.C. §103(a) as being unpatentable over Illera *et al.*, alleging that although it discloses the maturation of oocytes *in vitro* instead of *in vivo,* the oocytes will enter MII prior to fertilization. The Examiner also alleges that variations in the concentration of compounds is *prima facie* obvious.

Applicants traverse. As stated above, Applicants note that the results described in Illera *et al.* clearly demonstrate that when exogenous hormones, such as FSH and LH, are added to the culture medium, the fertilization rate actually decreases upon the addition of both EGF and IGF-1. In fact, only when FSH and LH, plus porcine follicular fluid are left out of the medium, do EGF in combination with IGF1 augment the fertilization rate. This is in direct contradiction to the present invention and thus, teaches away from the addition of both EGF and FSH. Applicants also note that the present invention does not comprise the use of IGF1. Thus, Applicants assert that Illera *et al.* does not render the present invention unpatentable. Accordingly, Applicants request reconsideration and withdrawal of the present rejection.

CONCLUSION

In view of the above, it is respectfully submitted that the application is now in condition for allowance and issue. The Commissioner is hereby authorized to charge any fees in connection with this application and to credit any overpayments to Deposit Account No. 14-1447. The Examiner is invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

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